REMARKS

Claims 8-27 are pending. Claims 8-15, 20 and 30 are withdrawn. Claims 16-19 and 21-27 are under consideration. Claim 16 has been amended to clarify that the array is a "non-cell based" array and that at least one "immobilized functional" cytosolic accessory protein is attached to the array surface. Support for these amendments is found in the specification as originally filed, for example, at p. 12, lines 24-28 (non-cell based) and at p. 3, line 18 and p. 6, lines 12-14 ("immobilized functional"). The specification at page 12, in contrasting the present invention with other, cell-based assays, makes clear that the present arrays are non-cell based protein arrays. This is further evident from the description of the array surface, e.g. at page 12, lines 7-11, which does not include a surface, such as a nutrient agar, which can be used for growing a cell, as in the yeast two hybrid assay. No new matter is introduced by these amendments.

Rejections under 35 USC 102(b)

Claims 16-19, 21, and 27 are rejected as anticipated by Wang et al., JBC 271:23811-17, 2006 ("Wang"), as evidenced by Gulbis et al., Cell 97:943-52, 1999 ("Gulbis"). The rejection is traversed as it applies to the amended claims.

Claim 16 as amended specifies that the array is a non-cell based array comprising a surface having attached thereto at least one immobilized functional cytosolic accessory protein of a membrane protein. Wang does not describe a non-cell based array comprising a surface having attached thereto at least one immobilized functional cytosolic accessory protein of a membrane protein, as required by claim 16. Rather, Wang describes a yeast two hybrid system to study the interaction of Kv α and β subunits of ion channel proteins.

Assuming, *arguendo*, that the Examiner's characterization of Wang as describing a voltage-gated potassium channel beta 1.3 subunit indirectly physically attached to the agar plate via the yeast cell is correct, this is not a non-cell based array. Instead, Wang describes only a conventional yeast two hybrid system which is referred to in the current application as

"cumbersome." Further, as explained in the Applicants' previous response, in the absence of the other subunits, the voltage-gated potassium channel beta 1.3 subunit will be expressed in the cytoplasm within the yeast cell, and therefore will be free to migrate within the cell. Thus, Wang does not describe an immobilized functional cytosolic accessory protein as required by the claims.

Wang therefore fails to describe the features of claim 16 and does not anticipate the claimed invention. For the same reasons, Wang fails to describe the remaining claims subject to the rejection, as claims 17-19, 21, and 27 depend from claim 16. Applicants request reconsideration and withdrawal of the rejection for anticipation.

Rejections under 35 USC § 103(a)

Claims 16-19 and 21-27 are rejected as unpatentable over Wang as evidenced by Gulbis in view of Charych et al. II, US Patent No. 7,148;058 ("Charych"). The rejection is traversed to the extent it is applied to the claims as amended.

As set forth above, Wang, as evidenced by Gulbis does not describe or suggest a non-cell based array comprising a surface having attached thereto at least one immobilized functional cytosolic accessory protein of a membrane protein, as required by the amended claims. The Examiner suggests that it nevertheless would have been obvious for one of skill in the art "to analyze the Kv channel 13 beta 1.3 subunits of Wang by anchoring to the protein microarrays on mirrored substrates in the manner of Charych." Applicants disagree.

Charych describes the anchoring of isolated proteins onto a surface (for example, the Abstract states that "the protein array elements may be attached directly to an organic functionalized mirrored substrate by binding reaction between functional groups on the substrate (e.g. amine) and protein (e.g. activated carboxylic acid).")

Wang does not teach or suggest isolated protein subunits but simply teaches expression of the β subunit in the yeast two hybrid system, or in Xenopus oocytes. Wang does not describe the isolation of any of these β subunits. Still less does Wang disclose any way in which the subunits may be isolated.

Wang similarly does not describe or suggest a non-cell based array including an immobilized functional cytosolic accessory protein. Merely anchoring the yeast two-hybrid system of Wang to the mirrored substrate of Charych would not result in the claimed invention.

Furthermore, Wang is directed towards a yeast two-hybrid system for the analysis of Kv channel subunit interactions. Wang does not teach isolated protein subunits, but simply teaches expression of the beta subunit in the yeast two hybrid system. Charych is directed towards the anchoring of isolated proteins onto a mirrored substrate. There would be no motivation for the skilled person to combine the teachings of Wang with those of Charych since they are directed towards completely different protein analysis techniques. The yeast two-hybrid system used in Wang is necessarily a living cell based system which requires the co-expression of potential interacting protein partners both labelled with domains of the beta galactosidase gene, such that when both interacting protein partners are expressed in the same cell, the domains of the beta galactosidase gene are brought together and a functional beta galactosidase activity is present. This activity can be monitored in a living yeast cell. The Charych system is completely different from this, and relates to isolated proteins immobilized on a mirrored substrate. Even if the skilled person were to be motivated to isolate the expressed proteins from Wang, these proteins would be labelled with the beta galactosidase domains required for the use of the yeast two hybrid system. However to do so would be nonsensical since monitoring of protein interaction using this system relies on expression in living cells such as those used by Wang.

In addition Charych does not provide any teaching for attaching membrane-bound proteins or cytosolic proteins expressed in whole cells to a surface for use as a protein microarray. Therefore Wang and Charych cannot be combined to produce the claimed invention.

Applicants request reconsideration and withdrawal of the rejection for obviousness.

Applicants respectfully submit that the pending claims are in condition for allowance. Applicant submit a request for continued examination with this response, petition for extension of time, and fees for same.

Please charge any additional fees due, or credit any overpayment of same, to Deposit Account 50-0311, Ref.: 33694-508001US.

Sincerely,

Dated: June 4, 2010

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